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Sheet 1 of 8

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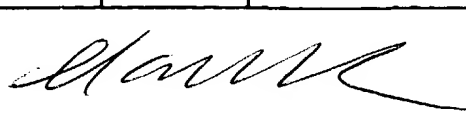
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1646**U.S. PATENT DOCUMENTS**

EXAMINER INITIAL	DOCUMENT NUMBER	DATE	NAME	CLASS	SUBCLASS	FILING DATE IF APPROPRIATE
W	BJ 5,759,811	06/02/98	Epstein et al.	435	69.1	11/13/96
	BK 5,223,408	06/29/93	Goeddel et al.	435	69.3	07/11/91
	BL 4,456,687	06/26/84	Howard Green	435	241	12/01/80
	BM 5,789,543	08/04/98	Ingham et al.	530	350	12/30/93
	BN 5,844,079	12/01/98	Ingham et al.	530	350	12/14/94
	BO 5,585,087	12/17/96	Lustig et al.	424	9.2	06/08/94
	BP 5,837,538	11/17/98	Scott et al.	435	325	10/06/95
	BQ 5,747,507	05/05/98	Ikegaki et al.	514	312	08/10/93
	BR 5,643,915	07/01/97	Andrulis, Jr. et al.	514	279	06/06/95
	BS 5,519,035	05/21/96	Maiese et al.	514	309	07/02/93

**FOREIGN PATENT DOCUMENTS**

	DOCUMENT NUMBER	DATE	COUNTRY	CLASS	SUBCLASS	Translation	
						YES	NO
W	BT WO 90/02809	3/22/90	PCT	C 12P	21/00		
	BU WO 92/15679	9/17/92	PCT	C 12N	15/10		
	BV WO 94/28016	12/08/94	PCT	C 07K	13/00		
	BW WO 95/23223	08/31/95	PCT	C 12N	15/00		
	BX WO 95/18856	07/13/95	PCT	C 12N	15/12		
	BY WO 96/09806	04/04/96	PCT				
	BZ WO 96/11260	04/18/96	PCT	C 12N	5/00		
	CA WO 96/16668	06/06/96	PCT	A 61K	38/17		
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	CC WO 97/11095	03/27/97	PCT	C 07K	14/475		
	CD WO 97/45541	12/04/97	PCT	C 12N	15/12		
	CE WO 98/12326	03/26/98	PCT	C 12N	15/12		
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✓	CK	WO 99/00117	01/07/99	PCT	A 61K	31/00		
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	CN	WO 99/10004	03/04/99	PCT	A 61K	38/00		
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✓	CW	Anderson, R. et al., "Maintenance of ZPA signaling in cultured mouse limb bud cells", <i>Devel.</i> <b>117</b> :1421-1433 (1993).
	CX	Angier, N., "Biologists find key genes that shape patterning of embryos", <i>New York Times</i> , Jan. 11, 1994, C-1.
	CY	Basler, K. and G. Struhl, "Compartment boundaries and the control of <i>Drosophila</i> limb pattern by Hedgehog protein", <i>Nature</i> <b>368</b> :208-214 (1994).
	CZ	Basler, K. et al., "Control of cell pattern in the neural tube: Regulation of cell differentiation by <i>dorsalin-1</i> , a novel TGF $\beta$ family member", <i>Cell</i> <b>73</b> :687-702 (1993).
	DA	Bass, S. et al., "Hormone phage: An enrichment method for variant proteins with altered binding properties", <i>PROTEINS: Structure, Function, and Genetics</i> <b>8</b> :309-314 (1990).
	DB	Bejsovec, A. and E. Wieschaus, "Segment polarity gene interactions modulate epidermal patterning in <i>Drosophila</i> embryos", <i>Development</i> <b>119</b> :501-517 (1993).
	DC	Bienz, M., "Homeotic genes and positional signalling in the <i>Drosophila</i> viscera", <i>TIG</i> <b>10</b> :22-26 (Jan. 1994).
	DD	Bitgood, M. and A. McMahon, "Hedgehog and Bmp genes are coexpressed at many diverse sites of cell-cell interaction in the mouse embryo", <i>Dev. Biol.</i> <b>172</b> (1):126-138 (1995).
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	DF	Brand-Saberi, B. et al., "The ventralizing effect of the notochord on somite differentiation in chick embryos", <i>Anat. Embryol.</i> <b>188</b> :239-245 (1993).
	DG	Brockes, J., "We may not have a morphogen", <i>Nature</i> <b>350</b> :15 (1991).
	DH	Bumcrot, D. A. et al., "Proteolytic processing yields two secreted forms of sonic hedgehog", <i>Mol. Cell. Biol.</i> <b>15</b> (4):2294-2303 (April 1995).
	DI	Bumcrot, D. A. and A. McMahon, "Sonic hedgehog: Making the gradient", <i>Chem. Biol.</i> <b>3</b> (1):13-16 (Jan 1996).
	DJ	Bumcrot, D. A. and A. McMahon, "Somite differentiation. Sonic signals somites", <i>Curr. Biol.</i> <b>5</b> (6):612-614 (June 1995).
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DN	Curry, et al., "Sequence analysis reveals homology between two proteins of the flagellar radial spoke", <i>Mol. Cell. Biol.</i> <b>12</b> :3967-3977 (1992).
DO	Davidson, E. H., "How embryos work: a comparative view of diverse modes of cell fate specification", <i>Develop.</i> <b>108</b> :365-389 (1990).
DQ	Davis, A. P. and M. R. Capecchi, "Axial homeosis and appendicular skeleton defects in mice with a targeted disruption of <i>hoxd-1</i> ", <i>Devel.</i> <b>120</b> :2187-2198 (1994).
DS	Dickinson, W., "Molecules and morphology: Where's the homology", <i>TIG</i> <b>11</b> (4):119-120 (1995).
DT	Dingemans, M. A. et al., "The expression of liver-specific genes within rat embryonic hepatocytes is a discontinuous process", <i>Differentiation</i> <b>56</b> :153-162 (1994).
DU	Dollé, P. et al., "Coordinate expression of the murine <i>Hox-5</i> complex homeobox-containing genes during limb pattern formation", <i>Nature</i> <b>342</b> :767-772 (1989).
DV	Dollé, P. et al., "Disruption of the <i>Hoxd-13</i> gene induces localized heterochrony leading to mice with neotenic limbs", <i>Cell</i> <b>75</b> :431-441 (1993).
DW	Echelard, Y. et al., "Sonic hedgehog, a member of a family of putative signaling molecules, is implicated in the regulation of CNS polarity", <i>Cell</i> <b>75</b> :1417-1430 (1993).
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DY	Ericson, J. et al., "Sonic hedgehog induces the differentiation of ventral forebrain neurons: a common signal for ventral patterning within the neural tube", <i>Cell</i> <b>81</b> (5):747-756 (June 1995).
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EB	Fallon, J. F. et al., "FGF-2: Apical ectodermal ridge growth signal for chick limb development", <i>Science</i> <b>264</b> :104-107 (1994).
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ED	Fietz, M. et al., "The hedgehog gene family in <i>Drosophila</i> and vertebrate development", <i>Devel. (Suppl.)</i> :43-51 (1994).
EE	Forbes, A. J. et al., "Genetic analysis of <i>hedgehog</i> signaling in the <i>Drosophila</i> embryo", <i>Devel.</i> <b>119</b> (Suppl.):115-124 (1993).
EF	Francis, P. H. et al., "Bone morphogenetic proteins and a signaling pathway that controls patterning in the developing chick limb", <i>Devel.</i> <b>120</b> :209-218 (1994).
EG	Gallop, M. et al., "Applications of combinatorial technologies to drug discovery. 1. Background and peptide combinatorial libraries", <i>J. Med. Chem.</i> <b>37</b> (9):1233-1251 (1994).
EH	Gérard, M. et al., "Structure and activity of regulatory elements involved in the activation of the <i>Hoxd-11</i> gene during late gastrulation", <i>EMBO J.</i> <b>12</b> :3539-3550 (1993).
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EJ	Halpern, M. E., "Induction of muscle pioneers and floor plate is distinguished by the zebrafish <i>no tail</i> mutation", <i>Cell</i> <b>75</b> :99-111 (1993).
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	EM	Haramis, A. et al., "The limb deformity mutation disrupts the SHH/ FGF-4 feedback loop and regulation of 5' <i>HoxD</i> genes during limb pattern formation", <i>Devel.</i> <b>121</b> (12):4161-4170 (Dec. 1995).
	EN	Hardy, A. et al., "Gene expression, polarising activity and skeletal patterning in reaggregated hind limb mesenchyme", <i>Devel.</i> <b>121</b> (12):4329-4337 (Dec. 1995).
	EO	Harmon, C. S. et al., "Evidence that activation of protein kinase A inhibits human hair follicle growth and hair fibre production in organ culture and DNA synthesis in human and mouse hair follicle organ culture", <i>British J. Dermatol.</i> <b>136</b> :853-858 (1997).
	EP	Hatta, K. et al., "The cyclops mutation blocks specification of the floor plate of the zebrafish central nervous system", <i>Nature</i> <b>350</b> :339-341 (1991).
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	EU	Hooper, J. and M. Scott, "The <i>Drosophila patched</i> gene encodes a putative membrane protein required for segmental patterning", <i>Cell</i> <b>59</b> :751-765 (1989).
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	EW	Hynes, R. O., "Induction of midbrain dopaminergic neurons by Sonic hedgehog", <i>Neuron</i> <b>15</b> (1):35-44 (July 1995).
	EX	Ingham, P. W., "Signaling by hedgehog family proteins in <i>Drosophila</i> and vertebrate development", <i>Curr. Opin. Genet. Dev.</i> <b>5</b> (4):478-484 (Aug 1995).
	EY	Ingham, P. W., "Hedgehog points the way", <i>Current Biology</i> <b>4</b> (4):347-350 (1994).
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	FB	Ingham, P. W. et al., "Role of the <i>Drosophila patched</i> gene in positional signaling", <i>Nature</i> <b>353</b> :184-187 (1991).
	FC	Izpisua-Belmonte, J. -C. et al., "Expression of the homeobox <i>Hox-4</i> genes and the specification of position in chick wing development", <i>Nature</i> <b>350</b> :585-589 (1991).
	FD	Izpisua-Belmonte, J. -C. et al., "Expression of <i>Hox-4</i> genes in the chick wings links pattern formation to the epithelial- mesenchymal interaction that mediate growth", <i>EMBO J.</i> <b>11</b> :1451-1457 (1992).
	FE	Jiang, J. and G. Struhl, "Protein kinase A in hedgehog signaling in <i>Drosophila</i> limb development", <i>Cell</i> <b>80</b> (4):563-572 (Feb. 1995).
	FF	Jessel, T. M. and D. A. Melton, "Diffusible factors in vertebrate embryonic induction", <i>Cell</i> <b>68</b> :257-270 (1992).
	FG	Johnson, R. L. and C. Tabin, "The long and short of hedgehog signaling", <i>Cell</i> <b>81</b> :313-315 (5 May 1995).
	FH	Johnson, R. L. et al., "Patched overexpression alters wing disc size and pattern: transcriptional and post-transcriptional effects on hedgehog targets", <i>Devel.</i> <b>121</b> (12):4237-4245 (Dec. 1995).
	FI	Johnson, R. L. et al., "Ectopic expression of sonic hedgehog alters dorsal-ventral patterning of somites", <i>Cell</i> <b>79</b> (7):1165-1173 (Dec. 1994).
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	FM	Koonin, E., "A protein splice-junction motif in hedgehog family proteins", <i>Trends Biochem. Sci.</i> <u>20</u> (4):141-142 (April 1995).
	FN	Kornblitt, A. R. et al., "Primary structure of human fibronectin: differential splicing may generate at least 10 polypeptides from a single gene", <i>EMBO J.</i> <u>4</u> :1755-1759 (1985).
	FO	Kornfeld, R. and S. Kornfeld, "Assembly of asparagine-linked oligosaccharides", <i>Ann. Rev. Biochem.</i> <u>54</u> :631-664(1985).
	FP	Krauss, S. et al., "Expression of the zebrafish paired box gene <i>pax(zf-b)</i> during early neurogenesis", <i>Devel.</i> <u>113</u> :1193-1206 (1991).
	FQ	Krauss, S. et al., "A functionally conserved homolog of the Drosophila Segment polarity gene <i>hh</i> is expressed in tissues with polarizing activity in zebrafish embryos", <i>Cell</i> <u>75</u> :1431-1444 (1993).
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	FT	Lee, J. J. et al., "Secretion and localized transcription suggest a role in positional signaling for products of the segmentation gene <i>hedgehog</i> ", <i>Cell</i> <u>71</u> :33-50 (1992).
	FU	Lee, J. J. et al., "Autoproteolysis in hedgehog protein biogenesis", <i>Science</i> <u>266</u> (5190):1528-1537 (Dec. 1994).
	FV	Lee, S. J. "Expression of growth/ differentiation factor1 in the nervous system: Conservation of a bicistronic structure", <i>Proc. Natl. Acad. Sci. USA</i> <u>88</u> :4250-4254 (Year).
	FW	Levin, M. et al., "A molecular pathway determining left-right asymmetry in chick embryogenesis", <i>Cell</i> <u>82</u> (5):803-814 (Sept. 8, 1995).
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	FY	Lopez-Martinez, A. et al., "Limb-patterning activity and restricted posterior localization of the amino-terminal product of sonic hedgehog cleavage", <i>Curr. Biol.</i> <u>5</u> (7):791-796 (July 1995).
	FZ	Lumsden, A. and A. Graham, "Neural patterning: A forward role for hedgehog", <i>Curr. Biol.</i> <u>5</u> (12):1347-1350 (Dec. 1995).
	GA	Ma, C. et al., "Molecular cloning and characterization of rKik10, a cDNA encoding T-kininogenase from rat submandibular gland and kidney", <i>Biochem.</i> <u>31</u> (44):10922-10928 (1992).
	GB	Ma, C. et al., "The segment polarity gene <i>hedgehog</i> is required for the progression of the morphogenetic furrow in the developing <i>Drosophila</i> eye", <i>Cell</i> <u>75</u> :927-938 (1993).
	GC	Ma, C. and K. Moses, " <i>Wingless</i> and <i>patched</i> are negative regulators of the morphogenetic furrow and can affect tissue polarity in the developing <i>Drosophila</i> compound eye", <i>Devel.</i> <u>121</u> (8):2279-2289 (Aug. 1995).
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	GE	Maccabe, J. A. and B. W. Parker, "The target tissue of limb-bud polarizing activity in the induction of supernumerary structures", <i>J. Embryol. Exp. Morph.</i> <u>53</u> :67-73 (1979).
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	GN	Nakano, Y. et al., "A protein with several possible membrane-spanning domains encoded by the <i>Drosophila</i> segment polarity gene <i>patched</i> ", <i>Nature</i> <b>341</b> :508-513 (1989).
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	GP	Niswander, L. and G. R. Martin, "FGF-4 and BMP-2 have opposite effects on limb growth", <i>Nature</i> <b>361</b> :68-71(1993).
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	GR	Nohno, T. et al., "Involvement of the <i>Chox-4</i> Chicken Homeobox Genes in Determination of Anteroposterior Axial Polarity during Limb Development", <i>Cell</i> , Vol. <b>64</b> : 1197- 1205 (March 22, 1991).
	GS	Nohno, T. et al., "Involvement of the Sonic hedgehog gene in chick feather formation", <i>Biochem. Biophys. Res. Comm.</i> <b>206</b> (1): 33-39 (Jan. 1995).
	GT	O'Farrell, P. H., "Unanimity waits in the wings", <i>Nature</i> <b>368</b> :188-189 (1994).
	GU	Parisi, M. J. et al., "The role of the hedgehog/patched signaling pathway in epithelial stem cell proliferation: From fly to human", <i>Cell Res.</i> <b>8</b> :15-21 (1998).
	GV	Parr, B. A. et al., "Mouse Wnt genes exhibit discrete domains of expression in the early embryonic CNS and limb buds", <i>Development</i> <b>119</b> :247-261 (1993).
	GW	Patel, N. H. et al., "The role of segment polarity genes during <i>Drosophila</i> neurogenesis", <i>Genes &amp; Devel.</i> <b>3</b> :890-904 (1989).
	GX	Peifer, M., "The two faces of hedgehog", <i>Science</i> <b>266</b> (5190):1492-1493 (Dec. 1994).
	GY	Perrimon, N. et al., "Generating lineage-specific markers to study <i>Drosophila</i> development", <i>Develop. Genet.</i> , <b>12</b> :238-252 (1991).
	GZ	Perrimon, N., "Hedgehog and beyond", <i>Cell</i> <b>80</b> :517-520 (24 Feb. 1995).
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